August 13, 2002

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate
Eastman Chemical Company
P. O. Box 431
Kingsport, Tennessee 37662

Dear Dr. Deyo:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for methyl isopropyl ketone (MIPK), posted on the ChemRTK HPV Challenge Program Web site on April 2, 2002. I commend Eastman Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Eastman Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Methyl Isopropyl Ketone (MIPK)

SUMMARY OF EPA COMMENTS

The Sponsor, Eastman Chemical Company, submitted a test plan and robust summaries to EPA for Methyl isopropyl Ketone (CAS No. 563-80-4; MIPK) dated February 15, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on April 2, 2002.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. The submitter needs to provide measured values for a number of these endpoints instead of relying almost exclusively on estimated values.

2. Health Effects. All appropriate SIDS-level tests have been performed.

3. Ecological Effects. EPA considers the algal toxicity study adequate for the purposes of the HPV Challenge Program. The submitted ecotoxicity data for fish and daphnia are inadequate. Testing is needed for these two endpoints.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE METHYL ISOPROPYL KETONE (MIPK) CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter provided estimated values for all endpoints. EPA disagrees with the submitter's approach to these endpoints. Critical endpoints such as water solubility and vapor pressure should be measured values. The use of estimated values increases the level of uncertainty in subsequent modeling such as the fugacity calculation.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The test plan for these endpoints is adequate for the purposes of the HPV Challenge Program. The submitter supplied a technical discussion that MIPK would not be subject to hydrolysis because it does not contain hydrolyzable functional groups. Therefore, a stability in water test is not needed. EPA agrees with the submitter that MIPK would not be subject to hydrolysis.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate test data are available for all health endpoints for the purposes of the HPV Challenge Program. However, the submitter needs to supply a robust summary for the reproductive toxicity endpoint. HPV Challenge Program guidance states that when a study addresses multiple endpoints, robust summaries are needed for each endpoint.

Ecotoxicity (fish, invertebrates, and algae). The acute algal toxicity study, with mean measured concentrations, is adequate. However, the fish and daphnia acute toxicity studies are inadequate. These studies were performed under static conditions with nominal concentrations, and as reported in the algal study (up to 78.2 % loss), there was most likely a significant loss of test material through volatilization. Because of this substance's volatility, EPA suggests that all testing be done with measured concentrations in a closed system with no head space. Testing should follow the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD, June 2000-available on the OECD website at http://www.oecd.org./ehs/test/monos.htm).

Specific Comments on the Robust Summaries

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Fugacity. The input values used in the fugacity calculation need to be added to the robust summary.

Health Effects.

Repeated-Dose Toxicity. Although it is stated as "a full assortment of tissues," the submitter needs to define the specific tissues that were examined histopathologically.

Genetic Toxicity (in vitro). In both summaries, the submitter needs to list concentrations that were tested. The submitter also needs to provide the number of replicate plates per concentration for the reverse mutation in bacteria study and the number of metaphases per concentration that were examined for the chromosomal aberration assay.

Ecotoxicity.

Algae. Water hardness is the only missing data element and needs to be submitted if available.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.